REMARKS

The claims have been amended to recite that a cell based and humoral response is elicited and the polynucleotide has been specified to be in the form of a plasmid including a promoter. The target peptide is an antigen or fragment of an antigen of an infectious microbe. The immune response includes an IgG response and Th1 and Th2 responses. The basis for the changes made can be found throughout the application including the claims now canceled.

The Examiner is thanked for the helpful suggestions to eliminate the claim objections. Those changes have been made.

The claims have also been amended in order to address the formal matters which gave rise to the rejection under 35 U.S.C. 112, thereby rendering that rejection moot.

It is respectfully submitted that all of the prior art rejections can be withdrawn in light of the foregoing amendments. None of the claims are obvious over Felgner in view of Kirby optionally further combined with Weiner and/or Collins.

Felgner teaches new cationic lipids and their use in various applications, one of which is for transfecting polynucleotides into cells. The statements at column 4, lines 10-13 are very general. There is no reference here to material which generates a cell-based and humoral immune response to a target polypeptide. Furthermore, the reference to the use of lipids at this point is very broad and covers a variety of liposomal and non-liposomal systems. At column 7, lines 49-51, there is a reference to a polynucleotide coding for an immunogen but at this point, there is no reference to any particular delivery system. Later in this disclosure, particularly at column 8, line 21 et seq., there is a reference to preparing lipid vesicles and using the lipid vesicles to

facilitate the transfectional transport of bioactive agents into cells. However, there is no reference in this material to DNA encoding an immunogen nor is there any reference in that paragraph to the way in which the lipid vesicles and the active can be associated with one another.

Later in Felgner's description, namely at column 15, line 7 et seq., there is a description of forming liposomes in which a film of lipid is formed on a surface and then hydrated to form the liposomes. A bioactive agent is captured within the liposomes either by being present in the aqueous suspending solvent or by being mixed with lipid before forming the dry film. There is a reference in this paragraph also to example 12 where empty liposomes are formed by that general method.

While there is a reference to the bioactive agent in the description of Felgner, the first reference to polynucleotide which codes for an immunogen is at column 18, lines 30-33. However, there is no indication in this passage as to the means by which cationic lipid is associated with the polynucleotide.

The only reference formulating polynucleotide in the working examples can be found in Examples 13 and 15-20. In Example 13, the polynucleotide is associated with the cationic lipid by forming a complex. There is no step in the complex forming process which results in entrapment of polynucleotide into the intravascular space of the liposomes. Example 15 does not even describe how the lipids and polynucleotide is mixed and presumably, therefore, it is by the same process as in Example 13. This polynucleotide does not encode an immunogen.

This review of Felgner shows that there is no teaching or suggestion that cationic liposomes in which polynucleotides encoding immunogens are entrapped in the intravascular space. Nor is there any teaching in this reference of any in vivo

results. To the extent there are transfection experiments carried out, all were carried out on cell lines in vitro.

Applicant generally agrees with the Examiner's characterization of the Kirby reference with the exception of the implication that DNA encoded with an immunologic polypeptide may be included therein. Kirby is silent as to this aspect and that silence would mean, as a matter of law, that it would be improper to draw any conclusions therefrom. DNA vaccines had not been invented as of the date of the publication of Kirby. That means that polynucleotide encoding an immunologic polypeptide in a function manner was not a part of the prior art as the publication date of Kirby in 1984 and could not have been contemplated by the authors. Furthermore, the document which Kirby cross references as disclosing further information about the DNA used in the entrapment of table 1, namely reference number 9, indicates that the DNA is E. coli DNA and no other characteristics of the DNA is given. Kirby also fails to show that any activity of the entrapped DNA is retained. Further, no reference is made to the delivery of the DNA, much less than upon being delivered after administration in vivo, the DNA would have the expected activity.

Weiner is relied upon solely to teach methods of causing an immune response to an individual by injection of a polynucleotide encoding an immunogen. It is not asserted to, nor does it cure, the basic deficiencies in the combination of Felgner and Kirby.

Turning to the Collins reference, Applicant disagrees with any assertion that it teaches a method of making dehydration-rehydration cationic liposomes for the purpose of encapsulating nucleic acids. Collins does describe cationic lipids at column 4, lines 44-45, but this disclosure relates to lipids in general. It does not suggest that any particular lipids or classes of lipids are useful with any specific actives or classes of

actives. Although Collins describes nucleic acid at column 6, lines 45 and 47, those nucleic acids do not encode an immunogen. Instead, there is a specific reference to anti-sense oligonucleotides.

Collins describes a process which involves dehydration of a composition containing empty liposomes, followed by rehydration. It will be appreciated that this method does not involve the hydration in the presence of an active but rather the active is, as indicated at column 5, lines 3-9, mixed with the dried lipid powder. All of the working examples, including those examples with actives which are proteins, use that method. There is no teaching or suggestion in Collins of the dehydration-rehydration method of the present claims in which active and empty liposomes are combined in aqueous suspension and then the mixture is dehydrated.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

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Respectfully submitted,

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